## REMARKS

Claims 1-3, 11-12, 15-19, 24 and 25 were pending in the application. Claim 26 has been added. Accordingly, after the amendments presented herein have been entered, claims 1-3, 11-12, 15-19, 24-26 will remain pending.

Support for the new claim can be found throughout the specification. Specifically, support for new claim 26 can be found, for example, in Example 10.

*No new matter has been added.* Any amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

### *Withdrawal of Certain Rejections*

Applicants would like to thank the Examiner for the withdrawal of the rejection of claims 1-3, 12, 15-19, 24-25 under 35 U.S.C. 112, first paragraph, and the rejection of claims 3, 17, 19 and 24 under 35 U.S.C. 112, second paragraph.

### *Rejection of Claims 1-3, 11-12, 15-19, and 24-25 Under 35 U.S.C. § 112, First Paragraph*

The Examiner has rejected claims 1-3, 11-12, 15-19, 24-25 under 35 U.S.C. 112, first paragraph because, according to the Examiner, "the specification while being enabling for a method of identifying a compound which binds to Kv4.2 or Kv4.3 and/or modulates the potassium channel activity of Kv4.2 or Kv4.3, does not reasonably provide enablement for a method of identifying a compound which binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel." Specifically, the Examiner is of the opinion that

> the claims are directed to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment. Since the claims are directed to methods using biologically active fragments of PCIP 9q polypeptides, the claims encompass methods using variant proteins.

And further,

> [s]ince detailed information regarding the structural and functional requirements of the protein fragments are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims.
>
> Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicants traverse this rejection for the following reasons.

Applicants believe that the Examiner has mistakenly applied this rejection to claims 1, 2, 11, 12, 15, 16, 24, and 25. Applicants respectfully point out that these claims are directed to screening assays using one of a number of ***specific*** 9q PCIP polypeptides set forth in the claims. Applicants' claims specify that the 9q PCIP molecule used in the screening assays claimed is selected from the group consisting of SEQ ID NO: 14, 16, 18, 20, 26 and 28.

Since these claims are not directed to methods using biologically active fragments of PCIP 9q polypeptides, this rejection, as it applies to these claims is thereby moot. Applicants respectfully request that the Examiner reconsider and withdraw the rejection as it applies to these claims.

Applicants further bring to the Examiner's attention that the biologically active fragments in Claim 3 are fragments of Kv4 channels and not biologically active fragments of PCIP molecules. Further, based on the teachings in the specification, and the skill of one of ordinary skill in the art it would be routine to determine what fragments of Kv4 channels are biologically active.

Accordingly, since Claim 3 is not directed to biologically active fragments of PCIP 9q peptides, this rejection, as it applies to this claim is thereby moot. Applicants respectfully request that the Examiner reconsider and withdraw the rejection as it applies to claim 3.

Finally, the Examiner has rejected claims 17, 18, and 19 because these claims are directed to methods using biologically active fragments of PCIP 9q polypeptides. Applicants respectfully bring to the Examiner's attention that claims 17 and 19 specifically define the fragments of the 9q polypeptides that are contemplated for use in the claimed methods. Applicants specify that the biologically active fragments of 9q polypeptides are either fragments that comprise an EF domain, residues 68-252 of human 9q, or a potassium channel α subunit binding domain. Therefore, the claimed fragments are not "variants" but rather ***defined*** fragments of specific 9q polypeptides which one of ordinary skill in the art based on the teachings in the specification could generate using only routine methods.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as it pertains to claims 17-19.

***Rejection of Claims 1-3, 11-12, 15-19, and 24-25 Under 35 U.S.C. § 112, First Paragraph***

The Examiner has further rejected claims 1-3, 11-12, 15-19, and 24-25 under 35 U.S.C. 112, first paragraph because, "[t]he claims encompass a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel....since the claims do not set forth a functional limitation which is modulated, it would require undue experimentation for the skilled artisan to determine the function which is modulated by the compound."

Applicants respectfully traverse this rejection.

Based on the teachings in the specification, an ordinary skilled artisan would be able to determine the function which is to be modulated by the test compound. Applicants provide working examples in which the activity of Kv4 potassium channels is monitored. For example, Applicants teach that Kv4 channel activities that can be monitored are the regulation of $I_{to}$ currents, regulation of peak current amplitudes, regulation of current density, regulation of inactivation time constants, regulation of recovery form inactivation time constants, and interaction with PCIP polypeptides (see, for example, Example 10).

Based on the teachings in the specification, and the general knowledge available to one of skill in the art, the claimed methods would not require undue experimentation to determine if a compound modulated the activity of a Kv4 potassium channel.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

***Rejection of Claims 1-3, 11-12, 15-19, 24-25 under 35 U.S.C. 112, First Paragraph***

The Examiner has rejected claims 1-3, 11-12, 15-19, 24-25 under 35 U.S.C. 112, first paragraph as, "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner believes that

> [t]hese are genus claims. The claims are drawn to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment.

Applicants respectfully traverse this rejection.

As indicated above, the only claims that are directed to methods using biologically active fragments of 9q PCIP molecules are claims 17-19. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection as it pertains to claims 1-3, 11, 12, 15, 16, 24, and 25.

As this rejection applies to claims 17-19, Applicants respectfully submit that the claimed genus is directed to ***specific*** fragments of PCIP molecules which are described in detail in the specification as filed. The claimed fragments are biologically active fragment of a 9q PCIP polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 16, 18, 20, 22, 24, 26, and 28, wherein said biologically active fragment is selected from the group consisting of an ***EF domain, residues 68-252 of human 9q and a potassium channel α subunit binding domain***. (*Emphasis added).*

Applicants respectfully submit that there is sufficient written description in Applicants' specification regarding the specific fragments of the PCIP molecules currently claimed, to inform a skilled artisan that Applicants were in possession of the claimed invention at the time the application was filed, as required by section 112, first paragraph.

Applicants' specification teaches that the PCIP molecules of the invention have calcium binding motifs, i.e., EF domains. For example, Applicants teach, in Example 12 that PCIP molecules contain calcium binding domains and map these domains within the polypeptide in

Figure 21. Applicants teach in Figure 41 the specific amino acid residues that are involved with calcium binding. Further, Applicants provide examples of a mutational analysis of EF domain residues in Example 10 to confirm that the residues that are described are in fact part of the EF domain.

Applicants teach in Example 10 that a fragment of KChIP2 denoted KChIP2Δ2–67 was produced to confirm that the C-terminal domain was sufficient to modulate Kv4 current density. This example demonstrates that a fragment of human 9q comprising amino acid residues 68-252 is capable of modulating Kv4 currents. The results of this experiment further indicate that Applicants were in possession of this fragment at the time of filing the instant application.

Lastly, Applicants specification teaches in Example 10, that the C-terminal domain is sufficient to interact with and modulate the current density of Kv4.2 in a way that is indistinguishable from full length 9q. Accordingly, Applicants demonstrate that the C-terminal domain, defined at page 49, lines 36-37 of the specification as the C-terminal 185 residues of human 9q, is capable of interacting with a potassium channel α subunit.

Based on the above teachings and working examples, one of ordinary skill in the art would understand that Applicants were in possession of the claimed fragments at the time the Application was filed. Further, the teachings in the specification are more than adequate to allow one of ordinary skill in the art to identify similar domains in corresponding polypeptide using only routine experimentation. Using sequence alignment programs (for example, the one described in Example 18) the ordinary skilled artisan could easily identify corresponding domains, e.g., EF domains, in related PCIP molecules.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as it applies to claims 17-19.

## CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

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